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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/823,886 | 03/30/2001 | Martha K. Newell | C1102/7002(HCL) | 7558 |

7590 06/27/2005
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| EXAMINER |
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KALLIS, RUSSELL

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| ART UNIT | PAPER NUMBER |
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1638

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/823,886

Applicant(s)

NEWELL ET AL.

Examiner

Russell Kallis

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7,25-27,38-41 and 49 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7,25-27,38-41 and 49 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 August 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 5/21/01;1/22/02.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

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Art Unit: 1638

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/25/2005 has been entered.

Claims 7, 25-27, 38-41 and 49 are pending and examined.

Rejection of Claims 7, 25-27, 38-39, 41 and 49 under 35 U.S.C. 102(b) is withdrawn in view of Applicant's amendments and arguments.

Rejection of Claims 25-27, 38-41 and 49 under 35 U.S.C. 112, second paragraph is withdrawn in view of Applicant's amendments.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-27 and 39-41 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

Art Unit: 1638

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official actions mailed 12/22/2003 and 9/23/2004. Applicant's arguments filed 6/17/2004 and 3/25/2005 have been considered but are not deemed persuasive.

Applicant asserts that the identifying characteristics of the genus of UCP inhibitors are described in the specification in light of the factors set forth by the revised Written Description Guidelines (response page 5). Applicant has not described UCP binding peptides, UCP antibodies, UCP dominant-negative nucleic acids or UCP encoding nucleic acid sequences other than SEQ ID NO: 1, 3, 5 and 7-12 that would decrease the level of UCP expression or activity.

Applicant's assertion that the Written Description Guidelines state that it is sufficient to have disclosed any number of the factors listed on page 5 lines 7-10 of Applicant's response is incorrect because Applicant has mistakenly listed the level of skill and knowledge in the art as a factor. The Written Description Guidelines state clearly on page 8 that all disclosed distinguishing identifying characteristics are to be weighed in view of the level of skill and knowledge in the art to determine if one of skill in the art would recognize from the disclosure that Applicant was in possession of the claimed invention. Clearly, Applicant's disclosure does not provide support for a written description of the broadly claimed genus or genera of UCP inhibitors.

Applicant asserts that they are not claiming inhibitor molecules themselves but are claiming their use (response page 6). Since those molecules required to practice the invention as broadly claimed are not described methods claiming their use are not described as well.

Art Unit: 1638

Applicant asserts that the specification describes UCP antibodies and binding proteins because the specification lists commercially available UCP antibodies and one of those antibodies bound a plant UCP (response page 6 to page 7). There is no indication that any of the commercially available UCP antibodies function as inhibitors of UCP expression or activity.

Claims 7, 25-27, 38-41 and 49 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is maintained for the reasons of record set forth in the Official actions mailed 12/22/2003 and 9/23/2004. Applicant's arguments filed 6/17/2004 and 3/25/2005 have been considered but are not deemed persuasive.

Applicant asserts that the term plant is to be interpreted broadly to include algae (response page 7). The specification does not set forth a broad definition for plants that would encompass unicellular flagellar algae.

Applicant asserts that *C. reinhardtii* is used as a model for plant systems is incorrect (response page 7). Applicant's specification actually states that *C. reinhardtii* is used as a model for many systems, including photosynthesis and motility. Moreover, Applicant has not correlated decreasing cell wall, plasma membrane, or chloroplast UCP expression with any of the claimed effects of the claimed methods in any plant or in *Chlamydomonas reinhardtii*.

Applicant asserts that the Examiner has not conducted a full analysis of the *Wands* factors (response pages 7-10). Applicant is incorrect in this assessment of the enablement

Art Unit: 1638

rejections in the Official actions mailed 12/22/2003 and 9/23/2004. Moreover Applicant has not responded to the specific points raised with respect to a lack of enablement set forth below again.

The specification is not enabling for regulating fuel metabolism in a plant by regulating UCP expression; for a method of producing a nutritionally enhanced plant; or for a method of preventing infection in a plant by decreasing UCP expression or activity because it is well known in the art that oxygen reactive species are toxic to the plant and their role in preventing infection is to destroy areas of infection in a localized fashion. Applicant has provided no guidance for accomplishing any of these methods using the claimed UCP inhibitors. Further, the claimed UCP inhibitors have different mechanisms of action and the disclosure does not provide guidance for using the broadly claimed genus of UCP inhibitors.

Regulating fuel metabolism in a plant is a complex process involving pathways that are subject to regulation of activity to maintain homeostasis with their environment. Applicant has provided no working examples for regulating fuel metabolism in a plant. The specification supports redirecting metabolic activity towards thermogenesis on page 9, lines 1-9; but does not teach how this can be achieved using the claimed inhibitors and thus the method is not enabled.

The presence of multiple isoforms of a single UCP gene family when attempting to alter UCP expression or activity using chemical or antisense inhibitors is unpredictable because although many UCP proteins may have a common function they may have different coding sequences and one may escape inhibition by antisense when using the other as the inhibitor.

Another unpredictable aspect when attempting to engineer expression or activity in a plant arises when protein isoforms have different regulatory properties wherein one isoform is not responsive to an external stimulus that would inhibit other gene family members. This is demonstrated in the

Art Unit: 1638

analysis of two UCP proteins in *Arabidopsis* where the two UCP proteins have similar sequence identities but different responses to chilling, suggesting that they would have different responses to inhibition by means other than chilling (Watanabe A. *et al.* Plant Cell Physiology, 1999, Vol. 40, No. 11; pages 1160-1166; see page 1166 column 2, last paragraph).

Plants having high levels of oxygen reactive species are not considered nutritionally enhanced, but are viewed by one of skill in the art to be compromised with respect to their nutritional value. Applicant has argued on page 10 of the specification that decreasing the activity of UCP in a plant will increase the yield of fat in a plant. It is not clear what Applicant means by fat. Nonetheless, increasing the yield of fat in a plant is not recognized as nutritionally enhanced. Further, Applicant merely recites that decreasing UCP expression or activity in a plant will produce a nutritionally enhanced plant (specification page 4, lines 30-32). Since, the disclosure does not provide guidance for applying any of the claimed inhibitors to achieve this effect, the specification does not provide adequate support for a nutritionally enhanced plant. Moreover, it is generally considered in the art that increasing the number of antioxidant species in a plant will actually increase the nutritional value of a plant. The prior art corroborates this view by teaching that dietary components having antioxidant activity have been associated with reducing the effects of oxygen free radicals (Meydani M. Annals of the New York Academy of Sciences. 2001, April; Vol. 928: pages 226-235; see abstract). Furthermore, Applicant's attention is directed to Claim 49, drawn to preventing infection in a plant by decreasing the expression or activity of UCP in a plant in an amount to prevent an increase in oxygen free radicals to prevent infection in a plant. The specification on page 42, lines 6-16, teaches that increased UCP expression levels were directly correlated with decreases in reactive peroxide oxygen species

Art Unit: 1638

thereby suggesting that UCP functions to prevent increased levels of oxygen free radicals.

Clearly, the specification teaches the opposite of the claims, that a decrease in UCP expression or activity is correlated with a prevention of an increase in oxygen free radicals, and thus the specification is not enabling for a method of preventing an infection in a plant. The prior art corroborates this view wherein overexpression of UDP in tobacco was a requirement for a reduction of damaging oxygen reactive species (Brandalise M. *et al.* Journal of Bioenergetics and Biomembranes, 2003, Vol. 35, No. 3 pages 203-209; see page 204, last paragraph, col. 1).

Clearly both the disclosure and the prior art do not support Applicant's claim that decreasing the UCP expression or activity in a plant will prevent an increase in oxygen free radicals, and hence the disclosure is not enabling for preventing infection in a plant or producing a nutritionally enhanced plant.

See *In re Fisher*, 166 USPQ 18, 24(CCPA 1970) which teaches "That paragraph (35 USC 112, first) requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved."

Given the unpredictability in the art as to regulating plant fuel metabolism or decreasing UCP expression in a plant to enhance nutrition or prevent infection in a plant; the breadth of the

Art Unit: 1638

claims encompassing the use of a wide range of inhibitors for a variety of methods; the lack of guidance in the examples of the specification or in the prior art as to which inhibitors would best serve the invention and would decrease UDP activity in a plant; although one of skill in the art can readily apply inhibitors or introduce antisense nucleic acids one would not know based upon Applicant's disclosure which embodiments would be inoperable and predictable eliminated, and thus undue trial and error experimentation would be needed by one skilled in the art to test a multitude of non-exemplified inhibitors in a myriad of non-exemplified plants for regulated UDP expression to regulate fuel metabolism; or to reduce UDP expression or activity to enhance nutrition in a plant or to prevent infection in a plant, and thus alter the phenotype in a multitude of non-exemplified transformed plant species. Therefore, the invention is not enabled.

Further with respect to Applicant's assertions that one of ordinary skill in the art can reliably predict, make and test antisense nucleic acid molecules and other inhibitors because numerous model systems were available at the time of filing to determine the effect upon UCP expression or activity, or to test the effect upon nutritional value, or to test for resistance to infection (response page 8), See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 41 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claim is drawn to non-transformed plants, which are a product of nature and not one of the five classes of patentable subject matter. See *American Wood v. Fiber Distintegrating Co.*, 90 U.S. 566 (1974), *American Fruit Growers v. Brogdex Co.*, 283 U.S. 2 (1931), *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 33 U.S. 127 (1948), *Diamond v. Chakrabarty*, 206 USPQ 193 (1980).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 7, 25, 38 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Allen M. *et al.* U.S. Patent 5,884,225 issued March 16, 1999.

The claims are broadly drawn to methods of regulating or decreasing UCP expression or activity in a plant by any means.

The reference teaches methods of harvesting crops and making corn meal (see Claims 33 and 38 and columns 1-2 and 4), wherein the UCP expression or activity is inherently decreased and therefore regulated upon harvesting; and thus the reference teaches all the limitations of Claims 7, 25, 38 and 49.

Claim Rejections - 35 USC § 103

Claims 7, 25-27, 38-41 and 49 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kowaltowski A.J. *et al.* FEBS Letters, 1998, Vol. 425; pages 213-216 in view

Art Unit: 1638

of itself. This rejection is maintained for the reasons of record set forth in the Official actions mailed 12/22/2003 and 9/23/2004. Applicant's arguments filed 6/17/2004 and 3/25/2005 have been considered but are not deemed persuasive.

Applicant asserts that the Examiner has not demonstrated that the reference teaches every element of the claimed invention because the reference does not teach regulation of UCP activity or decreasing the expression or activity of UCP in a plant cell wall, a plant plasma membrane, or plant chloroplast (response page 13).

In response to Applicant's argument that the reference does not teach the regulation of UCP activity or decreasing the expression or activity of UCP in a plant cell wall, a plant plasma membrane, or plant chloroplast, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the reference(s) would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

In response to Applicant's argument that the reference does not teach the regulation of UCP activity or decreasing the expression or activity of UCP in a plant cell wall, a plant plasma membrane, or plant chloroplast, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Moreover, the evidence of nonobviousness should be commensurate with the scope of the claims See *In re Lindner*, 173 USPQ 356 (CCPA 1972) and *In re Grasselli*, 218 USPQ 769 (Fed. Cir. 1983).

Art Unit: 1638

In response to Applicant's argument that there is no suggestion to combine the references or to modify the reference (response page 12), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, motivation to modify the invention is found in the reference and the art presented in the reference. The reference teaches that applying an inhibitor of UCP will result in the reduction of the production of oxidative radicals and it is well known in the art that this is beneficial to the plant by preventing cell death (see Abstract and Introduction of Kowaltowski). Moreover, Applicant is arguing limitations that are not in the claims. The only required step for performing the methods of the claims that have positive method steps is to contact the plant with a UCP inhibitor or to decrease the expression or activity of UCP. Since the mitochondria or mitochondrial membrane of the reference is from a plant, modifying the teachings of Kowaltowski to contact a plant with a UCP inhibitor to achieve the effect of inhibiting UCP expression or activity would have been obvious.

In response to Applicant's argument that Kowaltowski does not teach regulating fuel metabolism in a plant (response page 13) the recitation of "a method for regulating fuel metabolism in a plant" has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural

Art Unit: 1638

limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

All claims are rejected.

Art Unit: 1638

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (571) 272-0798. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

RUSSELL P. KALLIS, PH.D.
PATENT EXAMINER

Russell Kallis Ph.D.
June 2, 2005

Russell Kallis